# Asthma

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Pulmonary/Critical Care
Internal Medicine Academic Half Day
March 15, 2022

Banner
University Medical Center
Phoenix

The University of Arizona
College of Medicine
Phoenix

# OBJECTIVES

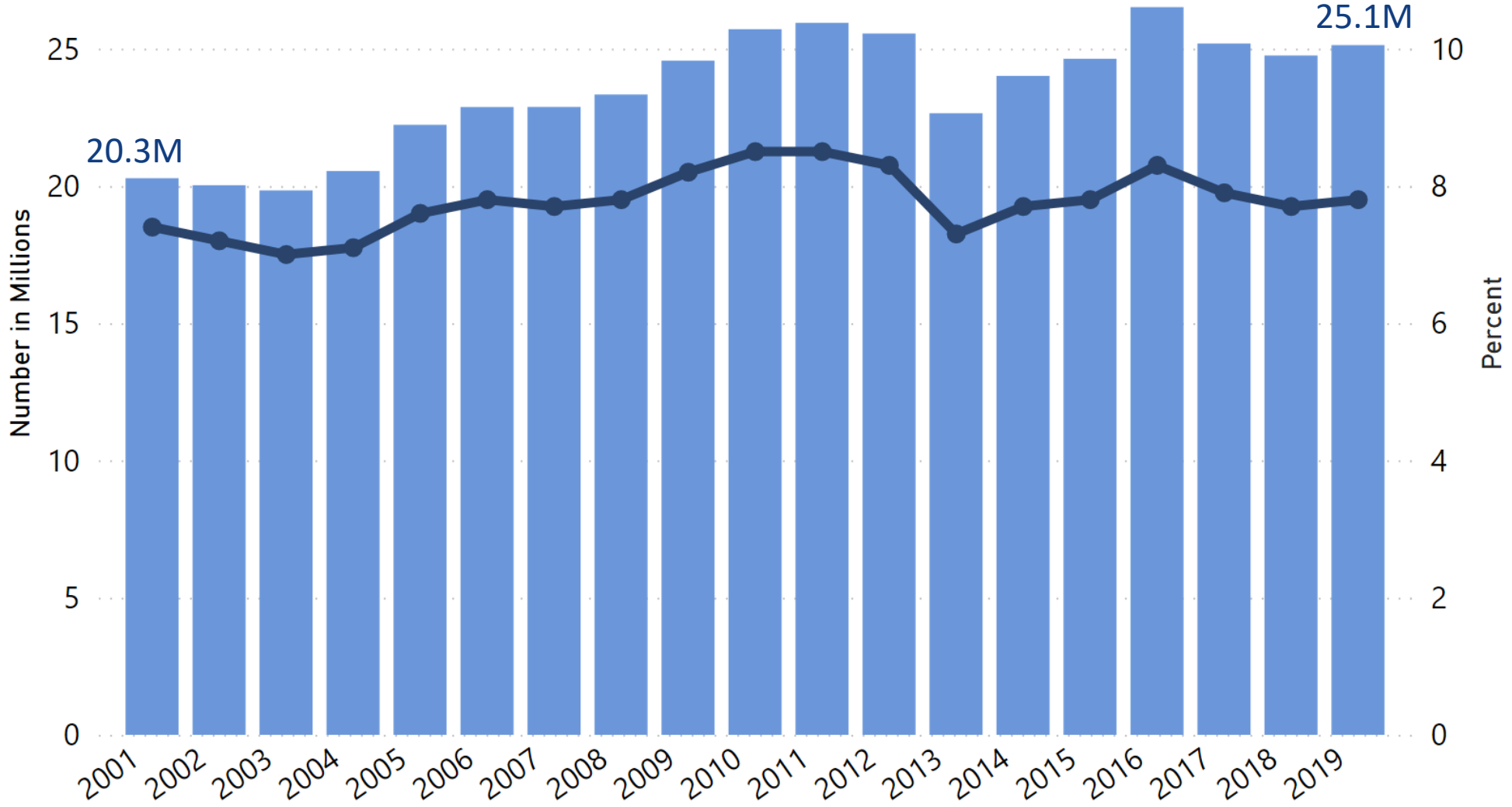
- Describe the different stages of Asthma Severity (intermittent and persistent)
- Know the recommended treatments for each stage of asthma severity and describe the step-up and step-down approach to management.
- Describe the diagnosis and management strategy of asthma exacerbation

# ASTHMA BACKGROUND

- Asthma is the most common chronic non-communicable disease, affecting over 260 million people globally in 2019
- Boys have a higher prevalence of asthma in childhood, woman have higher prevalence in adulthood
- Has higher prevalence in Black NH, and American Indian/Alaskan Native populations based on recent CDC data.
- Most of the morbidity and mortality associated with asthma is preventable .

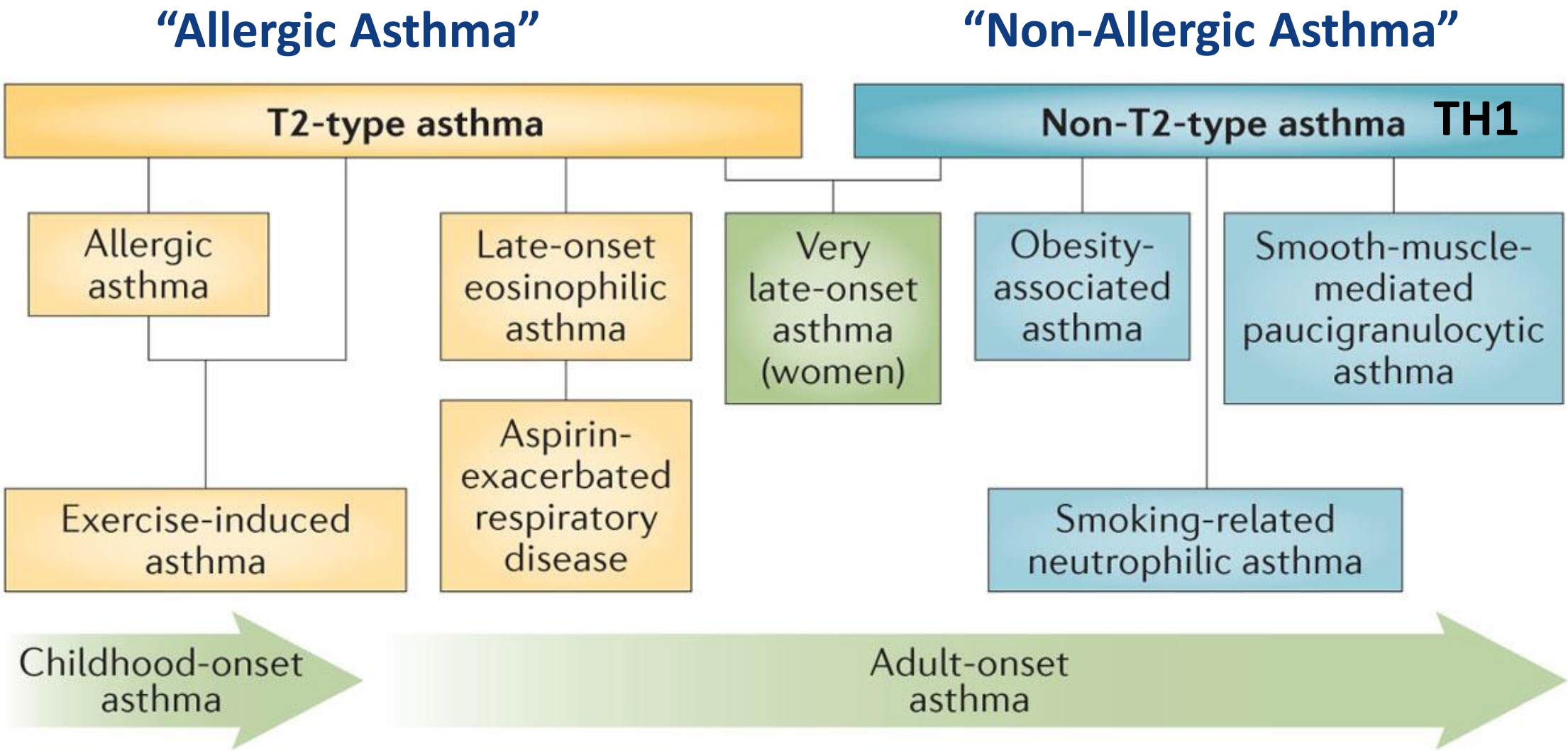
1. McCracken JL, Veeranki SP, Ameredes BT, Calhoun WJ. Diagnosis and Management of Asthma in Adults: A Review. *JAMA*. 2017;318(3):279–290. doi:10.1001/jama.2017.8372
Global Initiative for Asthma Global Strategy for Asthma Management and Prevention 2021

# Current Asthma Prevalence and Number of Cases (in Millions) by Year




Data from: https://www.cdc.gov

# ASTHMA PHENOTYPES




Holgate Nat. Rev. Dis. Primers 2015

# QUESTION #1

A 47-year-old man is evaluated in your internal medicine clinic for the first time, after having not seen a physician in over 5 years. He is an active smoker (1 pack a week), has a history of diet-controlled DM and hypertension.

You counsel him on smoking cessation, a DASH diet, and the need to get vaccinated against COVID due to his comorbidities (which he enthusiastically declines because he has a stockpile of Ivermectin his former naturopath gave him).

Just as you are about to walk out the door he says “Hey doc, I need a refill on my albuterol puffer for my shortness of breath”.

Realizing that you are about to be 30 minutes late for your next patient, you sit back down and find out that he has episodic shortness of breath multiple times a week with associated wheezing and cough. He uses his albuterol inhaler 5-6 times a week with improvement in his symptoms. Physical exam is unremarkable.

**Which of the following is the most appropriate next step in management?**

**A. Budesonide-salmeterol**
**B. Spirometry**
**C. Measurement of exhaled nitric oxide**
**D. Methacholine challenge testing**

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# CLINICAL FEATURES OF ASTHMA

- **There is no gold standard for the diagnosis of asthma. It is a clinical diagnosis based on history, patient characteristics, physical exam and the results of ancillary testing.**
- **History:**
  - Episodic nature of symptoms that often worsen at night, with seasonal changes in weather or after exposure to a trigger or allergen
  - Presence of triggers (environmental, cold, exercise, etc.)
- **Physical Examination**
  - High pitched wheeze, most commonly present during expiration and polyphonic (wheeze with several different tones) present throughout both lungs
  - Probability of asthma increases with presence of nasal polyps, atopic dermatitis, allergic rhinitis

# EVALUATION OF ASTHMA

- **Evaluation for functional airflow limitation is important in making the diagnosis in asthma**
- **Spirometry**
  - Airflow limitation- reduced FEV1/FVC (< 0.7)
  - Confirm Bronchodilatory Reversibility- improvement in FEV1 or FVC by 12% AND 200ml
  - Often associated with FEV1 variability between visits
- **Bronchoprovocation Testing**
  - Methacholine or Histamine Challenge- Fall in FEV1 > 20% and 200cc from baseline
  - Exercise Challenge- Fall in FEV1 >10% and 200cc from baseline

# ASTHMA DIFFERENTIAL DIAGNOSIS

- **Upper Respiratory Tract**
  - Vocal Cord dysfunction
  - Chronic upper airway cough
  - Obstructive Sleep Apnea
- **Lower Respiratory Tract**
  - COPD
  - A1AT deficiency
  - Cystic Fibrosis
  - Bronchiectasis
- **Gastrointestinal Tract**
  - GERD
- **Cardiovascular System**
  - Heart Failure
  - Congenital Heart Disease
  - Pulmonary Hypertension/ Chronic Thromboembolic Pulmonary Disease
- **Central Nervous System**
  - Habitual Cough
- **Medications**

*****~30% of adults with respiratory diseases have been misdiagnosed with asthma!***[2]**

McCracken JL, Veeranki SP, Ameredes BT, Calhoun WJ. Diagnosis and Management of Asthma in Adults: A Review. *JAMA.* 2017;318(3):279–290. doi:10.1001/jama.2017.8372

Aaron SD, et al. JAMA 2017, 317 (3): 269-279.

# QUESTION #2

That same patient from earlier presents for a follow up visit after having his spirometry performed.

He states that he continues to have intermittent “difficulty breathing”, chest tightness and wheezing when he has a physical day at work. Since last seeing you he had to visit the emergency department after he had a “breathing attack” at work. He was sent home with a course of steroids and now feels much better.

On physical examination, vital signs are normal. Oxygen saturation  is 97% with the patient breathing ambient air. Cardiopulmonary examination is normal.

Spirometry shows a normal forced vital capacity and no airflow obstruction. His FEV1 is 80% predicted.

**If this patient has asthma, which of the following tests is most likely to confirm your clinical suspicion of asthma?**

A. **Methacholine inhalation test**
B. **Exhaled Nitric Oxide Level**
C. **Elevated total Serum IgE level >500 IU**
D. **Lung  Volume Testing**

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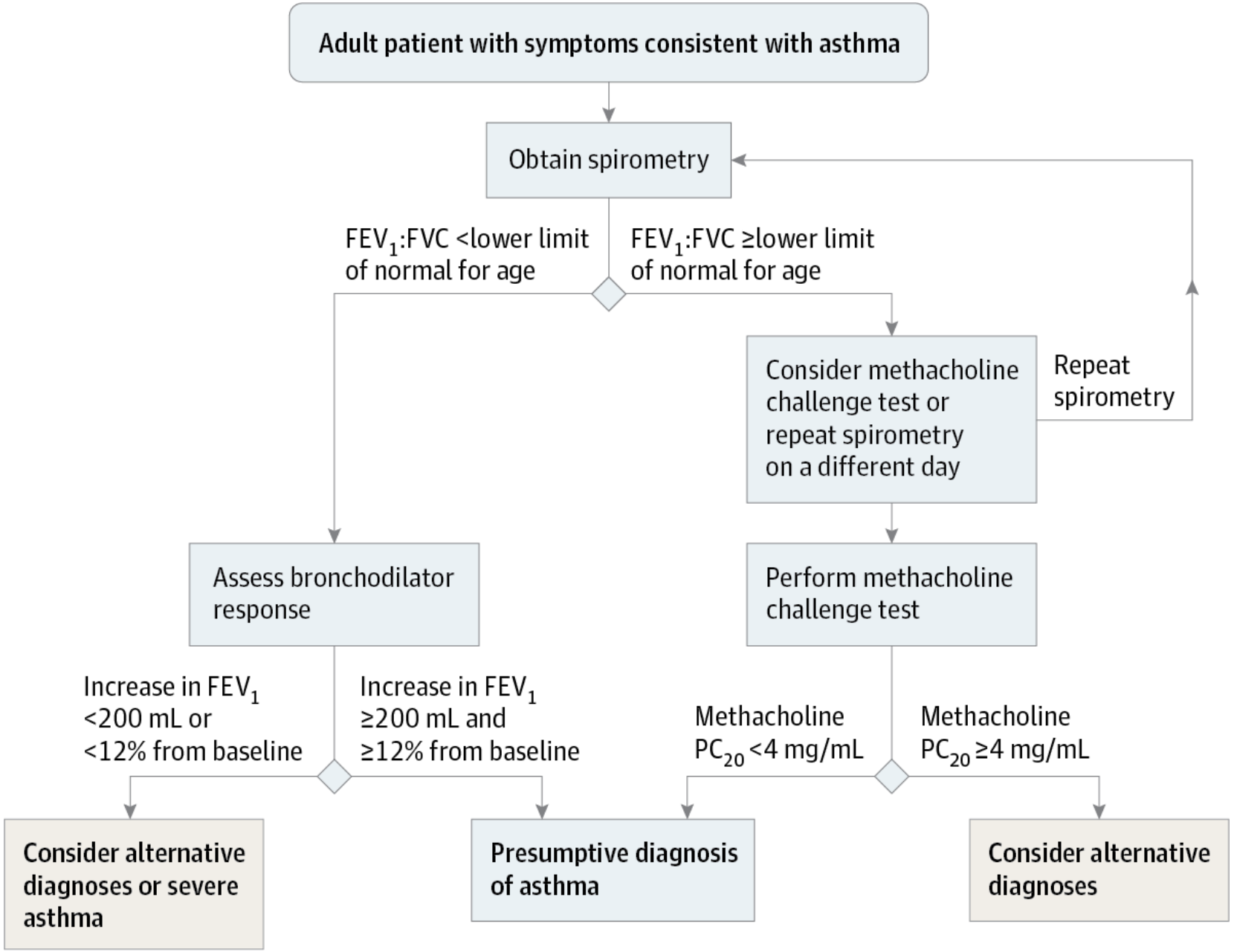


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# BRONCHOPROVOCATION TESTING

- **Used in patients with high clinical suspicion of asthma and normal spirometry**
- **Used for individuals who require an asthma screening for occupational reasons (i.e., military)**
- **Absolute Contraindications:**
  - Severe airflow limitation (FEV1 <50% or <1L)
  - MI or CVA in 3 months
  - Uncontrolled Hypertension (SBP >200mmgHg or DBP >100mmHg)
  - Known aortic Aneurysm
- **Can have false positives with Allergic Rhinitis, Bronchitis, HF, COPD and CF**

# METHACHOLINE CHALLENGE

- PD20/PC20 is defined as the dose or concentration of drug causing a 20% drop in FEV1
- ERS 2017 guidelines now favor PD20 over PC 20
- PD 20 < 400 micrograms suggestive of asthma (PC 20 <4)

| Severity | PD20 (micrograms) | PC20 (mg/mL) |
|---|---|---|
| Normal | >400 | >16 |
| Borderline | 100-400 | 4-16 |
| Mild | 25-100 | 1-4 |
| Moderate | 6-25 | 0.25-1 |
| Marked | <6 | <0.25 |

Coates AL et al. ERJ 2017

# QUESTION #3

**Which of the following concerning bronchoprovocation testing is most accurate?**

A. A positive methacholine challenge test accurately separates asthma from COPD
B. A negative methacholine challenge test has excellent negative predictive value in ruling out a diagnosis of asthma
C. Inhaled corticosteroid usage does not affect the sensitivity of the test
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# QUESTION #4

Back to our patient!

He returns to the clinic with positive methacholine challenge results suggestive of asthma (PD20 50 micrograms).

He states he is now having symptoms daily, requiring use of his albuterol inhaler. He wakes up at least twice a week from sleep due to difficulty breathing.

**How would you classify this patient's asthma?**

A. **Intermittent Asthma**
B. **Mild Persistent Asthma**
C. **Moderate Persistent Asthma**
D. **Severe Persistent Asthma**

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| Components of severity | | Classification of asthma severity (age ≥12 y) | | | |
|---|---|---|---|---|---|
| | | Intermittent | Persistent | | |
| | | | Mild | Moderate | Severe |
| Impairment | Symptoms | ≤2 d/wk | >2 d/wk but not daily | Daily | Throughout the day |
| | Nighttime awakenings | ≤2× mo | 3-4× mo | >1× wk but not nightly | Often 7× wk |
| | Short-acting $\beta_2$-agonist use for symptom control (not prevention of EIB) | ≤2 d/wk | >2 d/wk but not daily, and not more than 1× on any day | Daily | Several times per day |
| | Interference with normal activity | None | Minor limitation | Some limitation | Extremely limited |
| | Lung function<br>Normal $FEV_1$: FVC ratio<br>20-39 y 80%<br>40-59 y 75%<br>60-80 y 70% | • Normal $FEV_1$, between exacerbations<br>• $FEV_1$, >80% predicted<br>• $FEV_1$: FVC normal | • $FEV_1$, >80% predicted<br>• $FEV_1$:FVC normal | • $FEV_1$, >60% but <80% predicted<br>• $FEV_1$:FVC normal | • $FEV_1$, <60% predicted<br>• $FEV_1$:FVC reduced >5% |
| Risk | Exacerbations requiring oral systemic corticosteroids | 0-1/y | ≥2/y | ≥2/y | ≥2/y |
| | | Consider severity and interval since last exacerbation<br>Frequency and severity may fluctuate over time for patients in any severity category<br>Relative annual risk of exacerbation may be related to $FEV_1$ | | | |
| Recommended step for initiating treatment (see Figure 3 for treatment steps) | | Step 1 | Step 2 | Step 3 and consider short course of oral systemic corticosteroids | Step 4 or 5 and consider short course of oral systemic corticosteroids |
| | | In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly | | | |

McCracken JL, Veeranki SP, Ameredes BT, Calhoun WJ. Diagnosis and Management of Asthma in Adults: A Review. *JAMA*. 2017;318(3):279–290. doi:10.1001/jama.2017.8372

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## Rule of 2:

Symptoms less than 2 days a week
Less than 2 nighttime awakenings
SABA use less than 2 days a week

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## Moderate Persistent Asthma

## Daily symptoms
## Daily SABA Use
## >1X/week nighttime awakenings, but not daily

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**After having diagnosed our patient with moderate persistent asthma, which of the following is the best treatment for his symptoms?**

A. Tiotropium
B. Albuterol/Ipratropium Bromide
C. Budesonide/Formoterol
D. Prednisone taper, followed by albuterol PRN

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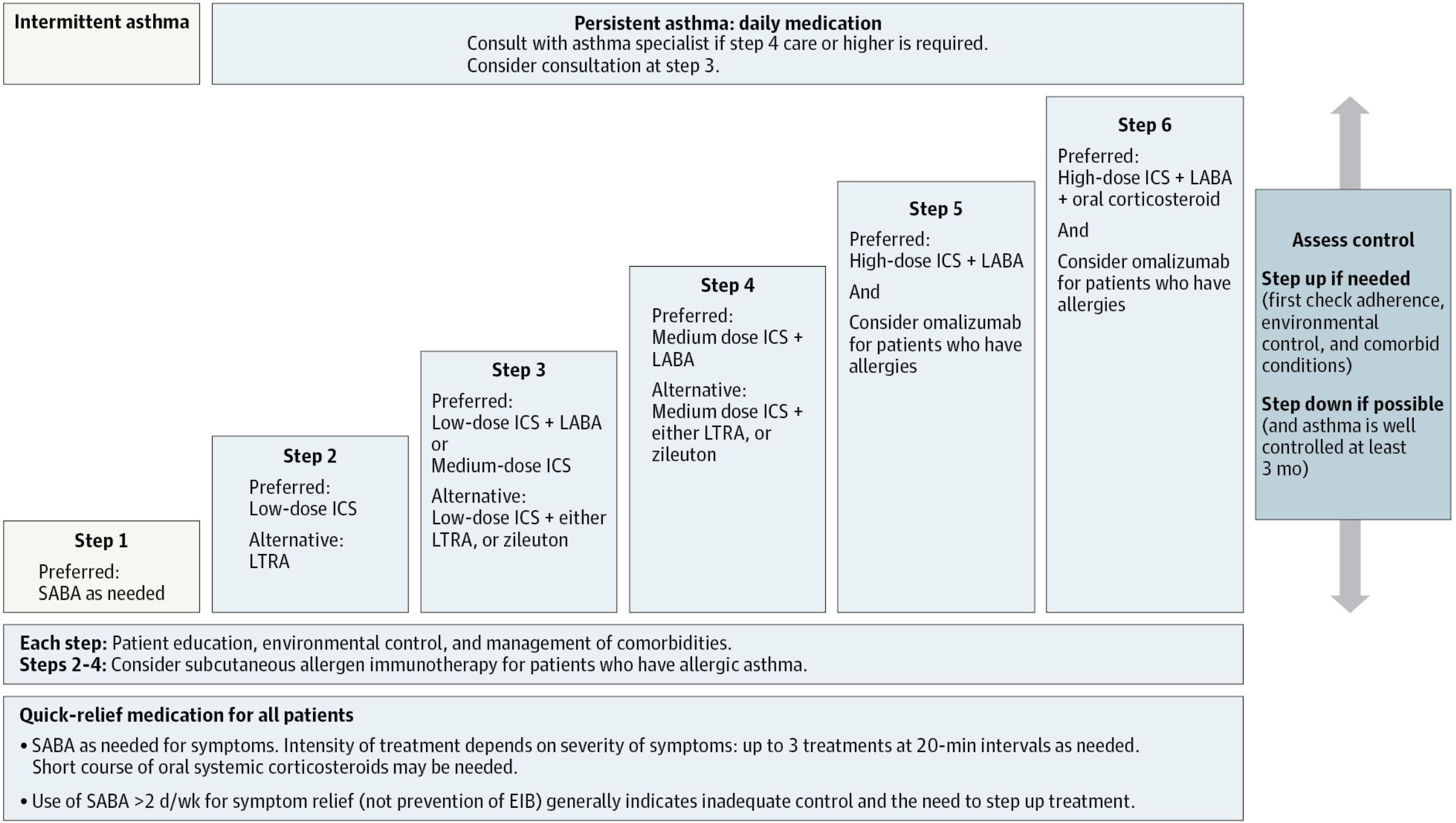
# GOALS OF ASTHMA MANAGEMENT

- Improve symptoms
- Improve lung function
- Reduce Exacerbations
- Reduce Rescue Medication administrations
- Reduce office and ED visits
- Reduce Treatment related adverse effects

Adapted from GINA 2021 Slide Set

# ASTHMA MEDICATIONS

- **Short Acting Beta Agonists (SABA)**
  - Albuterol, Levalbuterol
- **Long Acting Beta Agonists (LABA)**
  - Formoterol, Salmeterol.
  - NOT to be used as monotherapy
- **Long-Acting Muscarinic Antagonists (LAMA)**
  - Tiotropium
- **Inhaled Corticosteroids (ICS)**
  - Budesonide, Fluticasone, Mometasone
- **Leukotriene Inhibitors**
  - Montelukast, Zileuton
- **Glucocorticoids**
- **Azithromycin**
- **Biologics**

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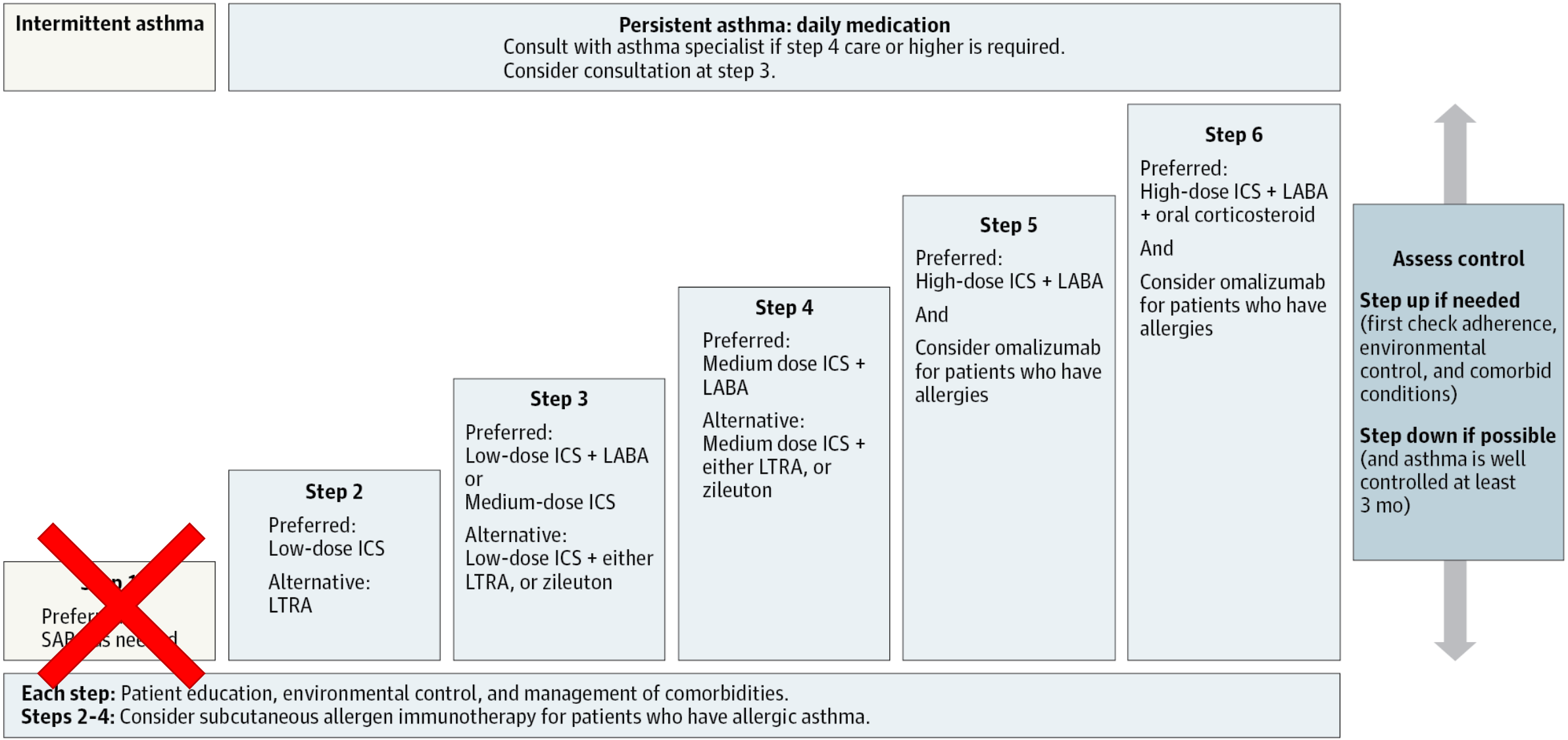


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# A KEY CHANGE IN ASTHMA MANAGEMENT

EDITORIAL
GINA 2019

## GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

# LANDMARK CHANGE IN ASTHMA MANAGEMENT

- **GINA no longer recommends SABA only treatment for step 1 in adults and adolescents**
  - There is evidence that SABA only treatment increases the risk of severe exacerbations, and that adding any ICS significantly reduces the risk
- **GINA now recommends that all adults and adolescents with asthma receive ICS-containing controller treatment to reduce the risk of serious exacerbations**
- **SABA alone associated with B-receptor downregulation, rebound hyperresponsiveness, decreased bronchoprotection**

Adapted from GINA 2021 Slide Set

# RISKS OF “MILD” ASTHMA

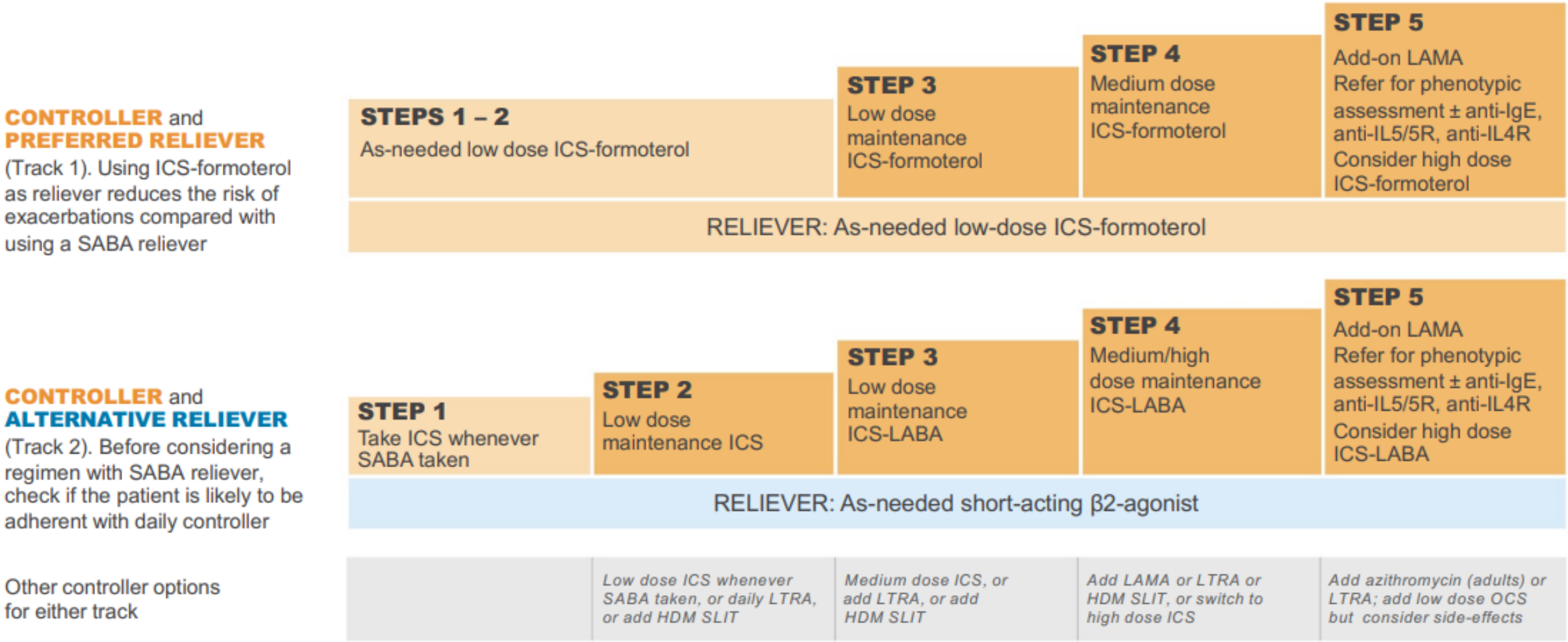
- **Patients with mild asthma are still at risk of serious adverse events**
  - 30-37% of adults with acute asthma exacerbation
  - 16% of patients with near fatal asthma
  - 15-20% of adults die of asthma

**Had symptoms less than weekly in the previous 3 months (Dusser, Allerg 2007)**

- **Exacerbation triggers are unpredictable (viruses, pollens, pollution, poor adherence, etc).**

Adapted from GINA 2021 Slide Set

# ASTHMA MANAGEMENT



# QUESTION #6

One year goes by and the same patient returns to the office after recently being hospitalized for an asthma exacerbation.

He feels better but continues to have dyspnea and intermittent wheezing. This is his second hospitalization within the past year for asthma exacerbation. He continues to take the budesonide/ formoterol inhaler that you prescribed him last year but is also taking tiotropium, Montelukast and prednisone which were started for him in the hospital.

On physical examination, vital signs are normal. Oxygen saturation  is 95% on ambient air. Pulmonary examination reveals expiratory wheezes with good air movement.

Laboratory studies reveal leukocyte count  of 10,000/µL with 650 eosinophils/µL. Serum IgE  level is 52 U/mL (normal range, 0-90 U/mL)

**Which of the following is the most appropriate treatment?**

A. **Change budesonide/formoterol to fluticasone/salmeterol**
B. **Initiate a trial of mepolizumab therapy**
C. **Initiate a trial of omalizumab therapy**
D. **Bronchial Thermoplasty**

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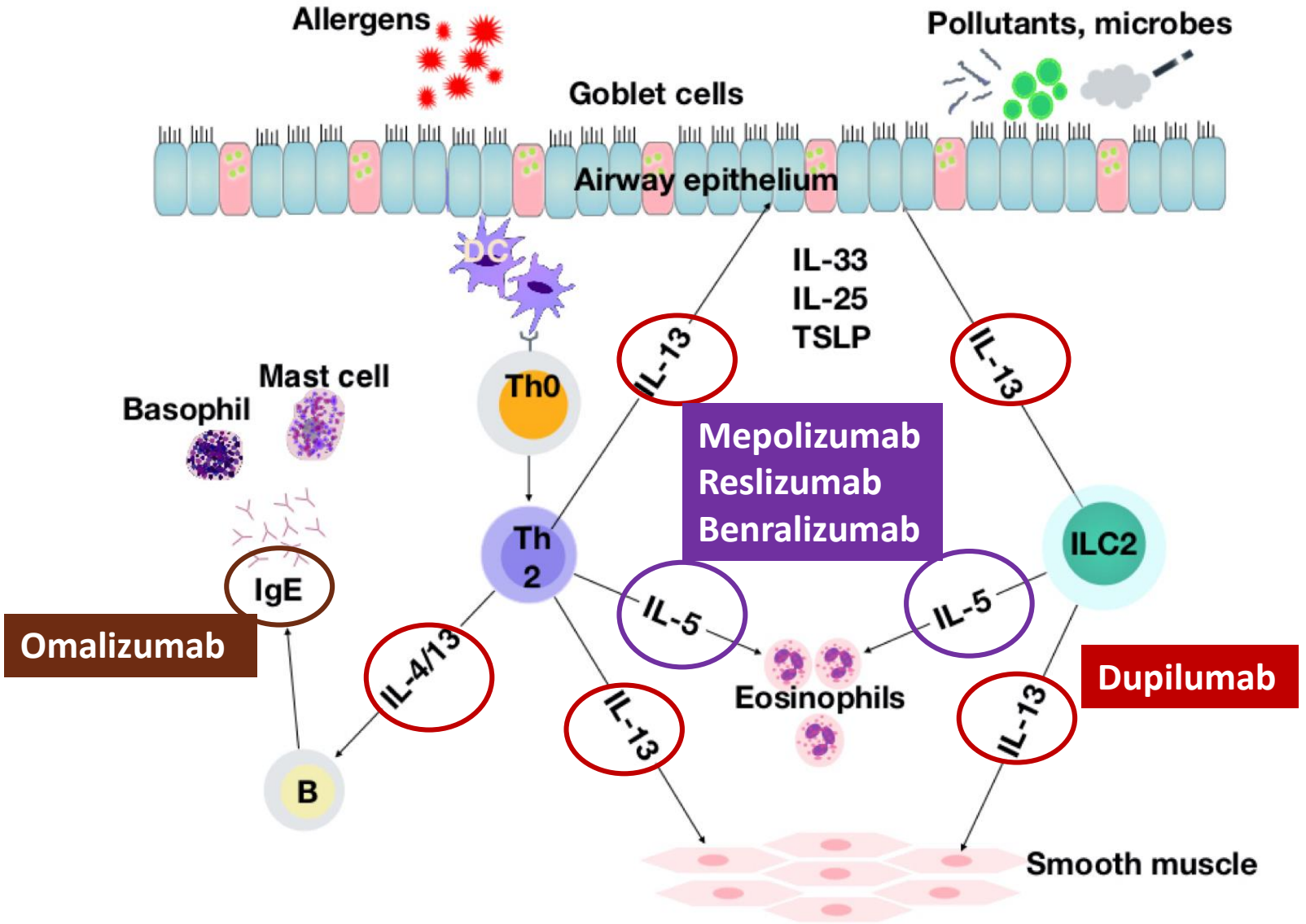
C. **Initiate a trial of omalizumab therapy**
D. **Bronchial Thermoplasty**




IL-4 Stimulates B Cells to synthesize IgE

IL-5 Regulates Eosinophil Production and maturation

IL-13 Leads to airway eosinophilia, airway fibrosis, mucous production and airway remodeling

IgE activates mast cells and basophils which produce leukotrienes that recruit and activate eosinophils

# MONOCLONAL ANTIBODY THERAPIES FOR TYPE 2 ASTHMA

| Drug | Dosing | Mechanism | FDA Indication |
|---|---|---|---|
| Omalizumab (Xolair®, Genentech) | 75-375 mg SC Q 2-4 weeks | Anti-IgE | Age ≥ 6 years with moderate to severe persistent asthma who test positive for year-round allergens[7] |
| Mepolizumab (Nucala®, GlaxoSmithKline) | 100 mg SC Q 4 weeks | Anti-IL-5 | Age ≥ 12 years with severe asthma and eosinophilic phenotype[8] |
| Reslizumab (Cinqair®, Teva) | 3 mg/kg IV Q 4 weeks | Anti-IL-5 | Age ≥ 18 years with severe asthma and eosinophilic phenotype[9] |
| Benralizumab (Fasenra™, AstraZeneca) | 30 mg SC Q 4 weeks x 3, then Q 8 weeks | Anti-IL-5Rα | Age ≥ 12 years with severe asthma and eosinophilic phenotype[10] |
| Dupilumab (Dupixent®, Sanofi/Regeneron) | 200 mg SC Q 2 weeks<br>300 mg SC Q 2 weeks | Anti-IL-4Rα | Age ≥ 12 years with moderate to severe asthma with an eosinophilic phenotype or with oral corticosteroid dependent asthma[11] |

Institute for Clinical and Economic Review, 2018
Evidence Report – Biologic Therapies for Treatment of Asthma

# QUESTION #7

A 32-year-old woman is evaluated for an asthma exacerbation. She previously had well-controlled asthma. She has increased the use of her maintenance inhaler and is using her rescue medication four times daily, but her symptoms persist. She reports no fever, chills, chest pain, or purulent sputum. She has no history of intubation, emergency department visits, or hospitalizations for asthma and has adhered to her medication regimen. She is a nonsmoker. Medications are inhaled budesonide and albuterol.

On physical examination, RR is 25/min, vitals otherwise normal. SPO2 96% on RA. Able to speak full sentences, has expiratory wheezes.

**Which of the following is the most appropriate treatment?**

A. **Doxycycline, 5-day course**
B. **IV methylprednisone, followed by 5 days of prednisone**
C. **Prednisone, 5-day course**
D. **Switch to budesonide/formoterol**

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# ASTHMA EXACERBATION

- Increase in baseline dyspnea, wheezing, chest tightness and cough. Decrease in lung function based on peak flow meter.
- Common triggers include viral infections, allergan exposure, air quality, seasonal changes and poor medication adherence.
- Venue for treatment depends on severity of symptoms including use of accessory muscles for respiration, chest hyperinflation, tachypnea, tachycardia, inability to complete sentences, etc.

Fergeson JE, Patel SS, Lockey RF. Acute asthma, prognosis, and treatment. J Allergy Clin Immunol. 2017;139:438-447

# CLINICAL CLUES FOR SEVERITY

**Mild to moderate exacerbation:**

- Talks in phrases or sentences
- Prefers sitting to lying
- Not agitated
- Respiratory rate 16 to 30 breaths/minute
- Heart rate 100 to 120 beats/minute
- $SpO_2$ >90%
- PEF >50% but <80% predicted or personal best

**Severe exacerbation:**

- Speaks in single words
- Sits hunched forward
- Agitated, diaphoretic
- Respiratory rate >30 breaths/minute
- Heart rate >120 beats/minute
- $SpO_2$ (on air) <90%
- PEF ≤50% predicted or personal best
- Eucapnia/ Hypercapnia

# OUTPATIENT ASTHMA EXACERBATION MANAGEMENT

- **Asthma Action Plan**
- **SABA (4-8 puffs every 20 minutes)**
- **ICS/LABA introduction**
- **PRN Oral Corticosteroid Prescription**
  - Typically, Prednisone 40-50mg for 5-7 days
- **Emergency Room Assessment if symptoms longer than 2-3 days or PEF <50-70% from baseline**

# ED/HOSPITAL ASTHMA EXACERBATION MANAGEMENT

- **SABA**
- **SABA/Ipratropium Bromide**
- **Magnesium Sulfate (2 grams)**
- **Continuous Nebulization**
- **Systemic Steroids, Usually intravenous if in extremis**
  - After discharge, 10-20% of patients with asthma exacerbations that are treated will have a relapse thus extended steroid course recommended.
- **Epinephrine** (for anaphylaxis)
- **Heliox**
- **NiPPV**
- **Intubation** (If PCO2 is high)
- **Paralytic, Inhaled Anesthetic, ECMO**

Fergeson JE, Patel SS, Lockey RF. Acute asthma, prognosis, and treatment. J Allergy Clin Immunol. 2017;139:438-447

# QUESTIONS?